With the writer's kind regards.

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THE

PERONEAL TYPE

OF

PROGRESSIVE MUSCULAR ATROPHY

A

THESIS FOR THE DEGREE OF M.D. IN THE UNIVERSITY OF CAMBRIDGE.

Read May 26th

BY

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Few subjects in neurology have undergone more searching revision of late years than the great clinical division known as Progressive Muscular Atrophy. Since Cruveilhier, Aran, and Duchenne first recognised it, it has been divided into many groups, clinically resembling, but pathologically distinct from, one another.

Such being the case it is necessary, before considering the immediate subject of this essay, to pass in review the several types into which the disease has hitherto been resolved.

The name *progressive muscular atrophy* was given to a classic group of cases now so well known as to render a description superfluous; but for the purposes of comparison, the following features must be noted. The commencement of the atrophy in the small hand muscles, thenar and hypothenar particularly, generally in the hand most used. The progression of the wasting up the arm to the shoulders, down the back, and the comparatively late affection of the lower extremities. The age of the patient is

generally advanced, but the disease may apparently begin at any time of life after twenty-one, *almost never* in childhood. Fibrillar tremors of the muscles are nearly always present. Contractures of certain muscles occur as late phenomena, giving rise to the well-known claw-shaped hand. The contractility to faradism is diminished in proportion to the wasting, but there is a tendency to the late development of polar alterations in the galvanic irritability, the so-called "*reaction of degeneration.*" This disease is very rarely, if ever, hereditary. The pathological changes at the seat of this disease are now generally admitted to consist of degeneration of the ganglion cells in the anterior horns of the spinal gray matter. It was for a long time considered by the early authorities to be an affection of the muscles, and not of the spinal cord. Cruveilhier it is true expected to find grave lesions of the central nervous system, and relates in telling language his astonishment at finding, in 1848, no disease of the cord as he had expected. However, in a subsequent case in 1853,* he found great thinning of the anterior roots, which we now understand to be secondary to disease of the anterior horns.

So again Aran and Duchenne at first considered the disease to be a myopathy, till in 1870 Duchenne with Joffroy† found and described disease of the anterior horns.

* Cruveilhier, *Arch. Gén. de Méd.*, 1853.

† Duchenne and Joffroy, *Arch. de Physiol.*, 1870, p. 449.

On the other hand Friedreich* as late as 1873 in his valuable monograph, takes up the opposite view; but then it must be noted that the cases he quotes in illustration of his views, in which he was able to make the autopsy, were none of them of the group now under consideration, but belong to types since shown to be myopathies, or else to the group of cases which form the subject of the thesis.

Now the above rapid sketch of what we may call the *myelopathic thenar type* of progressive muscular atrophy, is one of the most common, and as atrophy is its most prominent symptom, a very large number of cases have been, as it were, labelled with this name, and assigned to this group. Hence it is that we find in quite late writers, progressive muscular atrophy described as commencing at any age from three years upwards, often having no fibrillar tremors, and often distinctly hereditary.

As regards heredity, it must be noted that Bamberger,† Friedreich‡ and Leyden§ all hint at the tendency of the hereditary form to appear in the lower extremities. The subject is further complicated by the fact that apparently true myelopathies may commence in other than the thenar muscles.

* Friedreich, *Ueber Prog. Muskelatrophie*, 1873, Berlin.

† Bamberger, *Oesterr. Zeitung für Prakt. Heilk*, 1860. *Canstatt's Jahresbericht*, 1860, p. 88.

‡ *Op. cit.*

§ Leyden, *Klin. der. Rückenmarks Krankheiten*, 1875.

For instance, the shoulder muscles,* the serratus magnus,† the arm‡ and neck muscles§ have been described as being the point of attack of an affection apparently myelopathic in origin.

By the light of late observations aided by post-mortem examinations, the number of irregular or atypical cases is, however, becoming more and more narrowed.

Leaving the *myelopathic* form of muscular atrophy, we come now to the great group of *myopathies*, or cases in which the nervous system, central and peripheral, has remained perfectly intact, the affection being confined to the muscles only.

At the head of this group we have the now classical type of *myosclerosis*, familarly known as *Pseudo-hypertrophic muscular paralysis*. Duchenne considered this a pure myopathy, and nearly all subsequent authors agree with him, though a few have described changes in the spinal cord, which however cannot be considered primary.‖

The most striking points to be noted in myosclerosis are the following. Apparent hypertrophy of muscles sometimes associated with considerable atrophy. The leg muscles are generally first

* Schneevogt, *Niederlandsch. Lancet*, 1854. *Canstatt's Jahresbericht.* Duchenne, *L'Electrisation localisée*, 3e edit., p. 494 *et. seq.*

† Duchenne, *Ibid*, p. 496.

‡ Oppenheimer, *Habilitationschrift*, Heidelberg, 1855.

§ Erb and Schultze, *Archiv für Psychiatr.*, 1879, p. 369.

‖ Lockhart-Clarke, and Gowers, *Med. Chir. Trans.*, 1874.

affected, but not necessarily always. Contractures of groups of muscles make their appearance sooner or later, particularly those of the calf leading to talipes equinus. Absence of fibrillar contractions. Absence of polar electrical changes, but of course diminution of faradic irritability in proportion to the destruction of muscular fibres. The disease is essentially one of childhood, though exceptions to this have been recorded lately by Drs. Percy Kidd* and Fowler.† Lastly there is a very distinct tendency to heredity. Here then is a type of myopathy, combining the conditions *hypertrophy* and *atrophy*. Had it not been that hypertrophy was so marked and constant a symptom, the disease would in all probability have been classed from the beginning as a peculiar form of progressive muscular atrophy. In fact this has actually been the case as will be seen in considering the following type.

Closely allied to pseudo-hypertrophic paralysis is another form of myopathy, or rather probable myopathy, for as yet there are no accounts of post-mortem examinations forthcoming, except a doubtful case reported by Lichtheim,‡ of atrophy commencing in the neck and shoulder muscles, in which *post-mortem* there was found no disease of

* Kidd, "Pseudo-hypertrophic paral. in an adult," *St. Bartholomew's Hospital Reports*, 1881, p. 267.

† Fowler, *Clin. Soc. Trans.*, 1885.

‡ Lichtheim," Progr. Muskelatroph. ohne Erkrankung der Vorderhörner des Rückenmarks," *Arch. für Psychiatrie*, 1878.

the anterior horns at all. This class of cases was differentiated from the general mass of atrophies by Erb* in 1884, in a paper based on the clinical observation of twenty cases. This type, which he calls the "*juvenile form*" of progressive muscular atrophy, has distinct clinical features, by which it is easy to distinguish many cases among those of the older authors The salient features of this type may be summarized as follows. The age at onset is often in childhood, but usually about the time of puberty. The muscles usually affected first are the shoulder girdle and upper back muscles, very late if ever the forearm and hand muscles. Lower extremities often affected, but generally late. Hypertrophy of single muscles is very common, usually the deltoids, supra and infra-spinati, triceps, teretes, tensor fasciæ femoris, sartorius and calf muscles. There are never any fibrillar tremors, no reaction of degeneration, but a marked tendency to heredity. Though the diagnosis requires further confirmation by post-mortem examination, the disease is almost certainly closely allied to myosclerosis, and the very frequent occurrence of hypertrophy of single muscles lends colour to this view.

Here then we have the picture of a myopathy in which atrophy of muscles is the predominant feature, and hypertrophy an occasional one only, as

* Erb, "Ueber die juvenile Form der Progr. Muskelatroph.," *Deutsch. Archiv für Klin. Med.*, Bd. xxxiv.

opposed to myosclerosis where these conditions are reversed. Cases which answer to the above description occur frequently among the tables of collected cases by Wachsmuth,* Roberts† and other writers, among which may be mentioned Aran,‡ Eulenburg§ and Zimmerlin.‖

Another important group of myopathies remains to be noticed, and here our information concerning the pathology is more satisfactory.

Duchenne¶ in 1855 fully recognised the fact that progressive muscular atrophy, when it occurs in childhood, is possessed of quite peculiar features. He calls this the "*infantile form*" of progressive muscular atrophy. Though the disease is possessed of very marked distinctive features, it does not appear to have attracted any attention till 1874, when Landouzy** recorded the cases of two brothers suffering from this affection. MM. Landouzy and Déjerine†† in 1885, give the further history of these cases, and some others, with the account of a post-mortem examination. It may be thought strange that a disease, the symptomatology of which was

* Wachsmuth, *Zeitschr. für Rationelle Medicin*, 1855.

† Roberts, "*On Wasting Palsy*," 1858.

‡ Aran, *Arch. Gén. de Méd.* 1850, (case 7).

§ Eulenburg, *Deutsche Klinik*, 1856.

‖ Zimmerlin, *Zeitschr. für Klin. Med.*, Bd. 7.

¶ Duchenne, *L'électrisation localisée*, 3e edit., p. 518.

** Landouzy, *Société de Biologie*, Juin 27, 1874.

†† Landouzy and Déjerine, *Rev. de Médecine*, Feb. 1885.

known in 1855, should not have its pathogeny investigated till thirty years after.

This disease, as its name implies, is one of childhood or early adolescence. It has a distinct point of attack, namely the *muscles of expression.* One of the earliest phenomena is a fixed expression of countenance, owing to the immobility of the muscles of the upper half of the face. Then the forehead becomes smooth, and devoid of wrinkles, the eyes are never quite closed in sleep, and when the patient laughs his mouth extends laterally only, the rest of the face being unmoved (*"rire en travers"*). The lips are everted and pouting, and the whole appearance is so striking as to deserve the name *"facies myopathica"* given it by the French observers. The muscles of mastication and deglutition are quite free. Next attacked are the shoulder and upper arm muscles, except the spinati and subscapularis. The extensors of the forearm, the thenar and hypothenar, and interossei, and also the lower limbs, are affected, but late in the course of the disease. No hypertrophy of any muscles has as yet been noticed. The faradic irritability is diminished in proportion to the wasting, and there is never any reaction of degeneration. There are no fibrillar muscular movements, but there is a tendency to contractures of certain muscles. There is in this disease a very decided tendency to heredity, ascendant and collateral. Lastly, in the single case

in which MM. Landouzy and Déjerine were able to make an autopsy, the affection was found to be confined entirely to the muscles, the nervous system, peripheral as well as central, being absolutely free from disease. It may be here mentioned that Cruveilhier (*loc. cit.*) in 1853 describes two cases of general muscular atrophy, with affection of the face muscles, in which no disease of the spinal cord was found. Several well marked cases of this disease have been put on record, among which may be mentioned those of Remak,* Westphal,† Mossdorf,‡ Marie and Guinon,§ and Cénas and Douillet.‖

I now proceed to describe the cases illustrating the form of progressive muscular atrophy, which it is the object of this dissertation to establish as a distinct type ¶

* Remak, *Neurolog. Centralbl.*, No. 15, 1884.

† Westphal, *Berlin. Klin. Wochenschr.*, 1885, p. 617.

‡ Mossdorf, *Neurolog. Centralbl.*, No. 1, 1885.

§ Marie and Guinon, *Rev. de Méd.*, Oct. 1885.

‖ Cénas and Douillet, *La Loire Médicale*, 1885, p. 170.

¶ Since this thesis has been commenced, and some months after the lines, on which it was intended to work, had been laid down, there has appeared in the *Rev. de Médecine* for Feb. 1886, a paper by MM. Charcot and Marie on the same subject, illustrated by five cases. I take this opportunity at the same time, of acknowledging my indebtedness to M. Charcot for his able *Revue Nosographique* in the *Progr. Médical*, March 1885, which first directed my attention to the subject of amyotrophy.

Case I. *Progressive atrophy of the peroneal and tibial muscles, with resulting talipes varus. No fibrillar muscular tremors. No great loss of faradic irritability, but reaction of degeneration in some of the affected muscles.*

Harold B,* aged 7 years and 8 months. At the age of 6 years it was noticed that he dragged the left foot slightly, and that he began to walk on the outer part of the foot, in fact that a *talipes varus* was established, a condition which has been increasing ever since. It was also seen that this leg became smaller and weaker than the right. All this time he has been complaining of pains, which he cannot describe, in the legs, most in the morning when he gets up. He feels the cold in that leg very much. No tremors have been noticed nor do the legs jump at all at night. During the last 2 months the right leg has been getting thinner, and the same *varus* has been slowly making its appearance.

Family history.—He is one of twins, his twin sister is perfectly healthy and "twice as big as he is." He has two brothers, aged 17 and 15, quite strong and healthy. No history of a similar affection can be made out in any other member of the family on either side. Mother died of "cancer." Father is alive and well.

Present condition.—Small, pale, fragile looking child with an intelligent expression. His speech has been stuttering lately but he can whistle perfectly, has no deglutition trouble, the lips are not everted at all, and the tongue is protruded quite straight.

Upper extremities.—Thin and feeble, but apparently only sharing in the general low state of nutrition.

Trunk and spine natural.

* This case is one of Dr. Ormerod's to whose kindness I am indebted for the use of it.

Lower extremities.—The gluteal region and upper part of the thighs seem to be of natural volume and consistency considering the general feeble development.

FIG. 1.—*From a Photograph.*—The wasting being confined principally to the peronei and extensors, is more obvious on measurement than on a general view like this. The talipes varus is fairly well shown.

The thighs at about the middle, measure each 11 in. in circumference. But 2 in. above the patella the left is slightly the smaller of the two, thus, L.=8⅜ in., R.=8½ in. There is also some diminution in the circumference of the knee-joint, over the middle of the patella, thus, L.=8¼ in., R.=8¾ in.

There is a lively knee reflex, but no clonus.

Lower Leg.—Left calf fairly firm but smaller than right. Peronei, extensors and tibiales very flabby in the left side, less so in the right. Well marked pes varus of left foot and commencement of the same condition in the right. This varus is not due to contraction of opposing muscles but to simple loss of power in the peronei. The foot can easily be brought to its natural position, but then lies very flat. The circumferential measurements of the calves are L.=7¾ in., R.=8⅜ in. Two inches above the ankles L.=4¾ in., R.=5¼ in. The left leg is very cold and rather livid, but sensation is perfect all over. There are no muscular tremors. All the muscles act well to faradism, but in the extensor longus digitorum, ACC=KCC.

This is a fairly typical example of the class of cases now under consideration. The features worthy of emphasis are the age of the patient, the point of attack, and the electrical reactions. No fibrillar tremors were noticed, but they seem to be as often absent as present in this disease.

Heredity in this and the succeeding case was not to be made out, but I shall hope to show from the accounts of recorded cases, that this is not by any means always the case.

Case II.—*Progressive atrophy commencing in the peronei presumably, but now most obvious in the right calf muscles, occasional involuntary jerking of the muscles of the thigh, some degenerative electrical changes, but no true reaction of degeneration.*

Kate E., aged 23, came to me at the Metropolitan Free Hospital with the history that she has been walking badly since she was fifteen years old. She has sprained her right ankle twice owing to the weakness of the right leg. During the last year this weakness has become more pronounced and the leg has wasted in the region of the calf very much. She has also felt a bruised feeling of the muscles, most, perhaps, in the thigh, and in the gluteal region over the site of the sciatic nerve, but there have been no actual pains. She says the muscles twitch occasionally, but no fibrillar tremors have been noticed.

There is no history of any similar affection in any of her family. She is married and has had two children, one still-born at seven months, the other also premature but lived three hours.

Present condition.—She is a healthy-looking young woman with a high colour and generally well-nourished appearance.

There is no wasting of face muscles or indeed of any muscles of the upper part of the body. The chest and heart yield no physical signs of disease.

Lower extremities.—Left.—Quite natural, of good firm consistence all over. Knee-jerk natural.

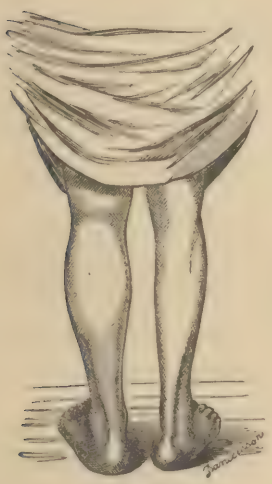

Fig. 2.

Fig. 3.

Right.—Thigh muscles very flabby particularly the anterior, but she has good power of extension and still better of flexion, circumference of right thigh rather less than that of left. Knee-jerk very feeble on right side.

Right lower leg.—Calf muscles extremely wasted, (Fig. 2) almost disappeared. Peronei, tibialis anticus, and extensor longus digitorum are all very flabby, but not so far gone as the calf muscles (Fig. 3). The small foot muscles do not seem to be much affected. She cannot stand on tip-toe on that leg at all, and the foot is very flat. Sensation is perfect, but the leg is always very cold, the contrast in this respect between this leg and the left is very striking. No fibrillar movements have been noticed.

Measurements.—Middle of right calf = 11 in. Left = $13\frac{3}{8}$ in. Right ankle 2 in. above malleolus = $7\frac{3}{4}$ in. Left = $8\frac{1}{4}$ in.

Electrical reactions.—To faradism the gastrocnemius will not react to the strongest currents. The peronei react fairly strongly, and so do the tibialis anticus and extensor longus digitorum. With the galvanic current the following results were obtained :—Gastrocnemius reacts to strong currents only, such as 40 milliamperes, and then only very feebly, but the KCC > ACC. Tibialis anticus, minimal contraction = 9 ma. and here KCC nearly equals the ACC. Extensor longus digitorum, KCC = 5 ma., ACC = 8 ma. Peroneus longus, KCC = 4 ma., ACC = 6 ma. It was not considered safe to use very strong currents, as the patient was three months advanced in pregnancy.

In this case the calf muscles are at present the seat of the most advanced changes, but the tendency to sprain the ankle as far back as the age of fifteen, suggests the possibility that the peroneal muscles may have been the earliest affected.

In addition to these cases I have two others, for which I am indebted to Dr. Gee and Sir Dyce Duckworth, in whose wards they were. Unfortunately, though I have spared no pains, I have been quite unable to trace them after leaving the hospital. Though the notes are scanty, the similarity of these cases to the type now under consideration must be my excuse for reporting them at second hand.

Case III.—Simon W., aged 49, a cigar-maker, was admitted into Luke Ward, St. Bartholomew's Hospital, in April, 1880. The notes are briefly these. At the age of 15 years his legs became weak and began to waste. This went on for 9 years and then the hand muscles, began to waste (? which hand).

For the last 18 years he has had a slowly increasing dorsal

angular curvature of the spine with some lateral deviation, which he attributes to carrying heavy weights, and is evidently not due to caries. There is no history of syphilis or lead poisoning. His mother had a similar affection of the legs. In walking, the toes drag. There is great atrophy of the tibialis anticus. The muscles of the calf are smaller than natural. There is no atrophy of any other muscles of the leg. Knee-jerk abolished.

Upper extremities.—Great atrophy of thenar and hypothenar muscles and probably interossei. All the other arm muscles seem natural. Marked fibrillar contractions in arms and legs.

The general resemblance of this to the preceding cases is apparent, but there are these important differences, the muscle of the leg first attacked is the tibialis anticus; the hand muscles are affected, which we shall see is a common incident in the later progress of the disease; there are marked musculomotor phenomena, and there is heredity.

Case IV.—Edward M., aged 46, a bricklayer, was admitted into John Ward, St. Bartholomew's Hospital, in June, 1884. He has had gradual wasting of the right leg 9 years. The leg is very weak and much colder than the left. There has been very little change for the last 3 years, but the difficulty in walking on it increases slowly. He has occasional cramps in the leg. Three weeks before admission he had been suffering from rheumatism, which he said has settled in the affected limb. No heredity can be made out. Has always been temperate.

Condition on admission.—Healthy looking man. Chest and upper extremities natural.

Lower extremities.—*Left* natural. *Right thigh* natural. *Right leg* and *foot* much wasted. Muscles on outer and anterior aspect of leg, more wasted than calf muscles. Tibialis anticus much wasted. Fibrillar contractions occasionally seen. Sensation

perfect. Right leg much colder than left. Tendon reflexes normal.

No reaction to faradism or galvanism in tibialis anticus and extensor longus digitorum, but peroneus longus, gastrocnemius and soleus act fairly well. Electro-sensibility lost over wasted muscles.

I think that these cases afford some proof of the existence of a distinct type of "progressive muscular atrophy," commencing in the *lower extremities*, and from the tendency of the affection to attack first the *peronei* and *extensors*, it is proposed to call the disease the "*peroneal type*" of progressive muscular atrophy, a provisional term which does not involve any theory as to causation.

It will not be out of place now to consider more in detail the several points on which the disease may be established as a separate type. In order to facilitate reference, there is appended to this essay a table of all the cases I have been able to collect, after rejecting many which were doubtful, owing to scanty reporting.

In the first place must be noticed the *age* at which the disease appears. Including the four cases above recorded, there are available in all, thirty-nine cases, many of the same family, as in those reported by Eichorst (Table, 10), where we have ten cases closely related to one another; as the age in some is only to be inferred, I have thought it better in this instance to give an average age for the whole family.

Arranging the ages then in quinquennial periods, the following results are obtained.

Ætat.	1-5,	-10,	-15,	-20,	-25,	37,	46.
Cases.	8,	10,	8,	10,	1,	1,	1.

By this will be seen that in thirty-six of the cases, the disease appears first at ages under twenty, and of these in twenty-six, or about sixty-six per cent., the onset of the disease occurs between the ages of two and fifteen, and though it is unsafe to draw definite conclusions from so small a number of cases, it is probable that these figures do not under state the case. The disease then is one of childhood.

Next as to *sex*, here we find twenty-eight males as opposed to sixteen females, the proportion of females being large compared with that in the myelopathic form, in which Roberts, for one, finds only fifteen female cases, out of a total of ninety-nine cases.

In estimating the influence of *heredity*, the arrangement of the figures must be somewhat altered, for of the total number it will be seen that many belong to the same family, and a family from the point of view of heredity must be regarded as an individual. It would obviously lead to an over estimation of the hereditary influence if each member of a family were considered as a separate proof of its existence. Regarded then from this stand-point we

have for consideration seventeen cases only, but of these a marked heredity exists in twelve.

Even therefore after taking these precautions against over-rating heredity, its influence is sufficiently obvious. The term heredity is used here in its widest sense and perhaps somewhat loosely. For the present purpose the appearance of the same disease in two or more children of the same parents is regarded as heredity. Some authors, Eichorst for instance, do not consider this collateral form as true heredity, but it seems that for the purpose of clinical distinction this form of heredity is as valuable as any other. Pure collateral heredity without any ascendent or descendent features, occurs in four or one-third of the above hereditary cases. (Table, 5, 7, 12, 17).*

The *mode of onset* has next to be considered. In *all* the cases the legs are first affected, and where any more accurate description of the order of affection is given, we find the peronei most often bear the first brunt of the attack. This is shown particularly well in Schultze's cases, (Table 12), which may be studied as the most typical instances of this form of disease. Here was noticed the appearance from day to day of a pes varus, not due to contracture of opposing muscles,

* For an interesting *resumé* of the subject of heredity consult Möbius, "Ueber der hereditären Nerven-Krankheiten," *Volkmann's Sammlung*, Bd. ii., Abth. i., No. 171.

but simply to loss of substance and power in the peronei. Closely associated with these, and probably next in order of affection are the extensors, the tibialis anticus, and the extensor longus digitorum. Lastly come the flexor muscles, the gastrocnemius, soleus and tibialis posticus. It must be borne in mind that though the peronei are most often affected, the disease may choose any of the above groups for its invasion. It is noteworthy that the small foot muscles do not seem to be ever the first attacked.

In the progress of the disease the upper extremities and small hand muscles are often affected, and comparatively early; in one of Schultze's cases about four years after the first symptom. This point is also emphasized by Charcot and Marie. It must be remembered that never is any hypertrophy of muscles present. There is considerable diversity of opinion as to the diagnostic significance of *fibrillar or fascicular tremors* of the muscles. Aran laid great stress on their importance in progressive muscular atrophy, he speaks of them as being "true nervous discharges." Duchenne on the other hand, perhaps rather under-rates their significance, when he states that he has noted their absence in one-fifth of the cases he has observed. This is no doubt true, but it is certain that many cases which Duchenne included under the term, progressive muscular atrophy, as for instance the "infantile

form," were not of nervous origin, but pure affections of the muscles, and whatever the true relations of the tremors may be to the nervous forms, it is quite certain that they are *never* present in the myopathic forms. It is very probable that in the true myelopathic form these tremors are rarely, if ever, absent.

In the peroneal type, however, they are absent in some typical cases and present in others. Thus, they are absent in nineteen cases, not mentioned in eight, and present in twelve cases. When present they are often described as being more than fibrillar tremors, namely, contraction of more or less large bundles of muscle; the resulting movement may then be called fascicular. Here may be related a case, which again I owe to the kindness of Sir Dyce Duckworth.

Case V.—*Marked fascicular twitchings of muscles of calves, often accompanied with severe pains. Some wasting of both calves. Same twitchings in peronei, but less marked. No other muscles affected. No electrical changes. Elder brother had same affection.*

Alfred L., aged 35, has been a butler, is now a coffee tavern keeper; was admitted to John Ward, St. Bartholomew's Hospital, in October, 1885.

For nine months he has suffered from constant twitchings and "flickerings" in the gastrocnemei muscles. During the same time the calves have been slowly diminishing in size, equally. When first attacked the tremors were accompanied by excruciating stabbing and pricking pains worse generally at

night. It was for these that he sought admission. He says he used to have a large calf, but has lost at least one inch in girth since the trouble began. No history of syphilis or intemperance. An elder brother had exactly the same condition extending over a period of four years, but has since died of some malarial fever in Canada. Another brother died of pneumonia in Canada. He has a sister living who has seven children healthy, but has lost two with "convulsions."

Present condition.—He is an intelligent, well made, healthy looking man. There is nothing noteworthy to be made out in the chest, or the muscles of the upper part of the body.

Lower extremities.—*Thighs* quite natural.

Lower leg.—Incessant contractions of bundles of muscle in the gastrocnemei. These contractions involve an unusually large area of the surface, reminding one rather of the effect of faradism with a small electrode. These movements can be occasionally seen in the peronei muscles, but much less frequently and of much less amplitude. Since he has been under treatment the pains have been much less, but they occasionally come on severely at night. When first seen there was complete loss of knee-jerk, but now (four months after admission) there is a feeble reflex on both sides, but decidedly less on the right. There is no diminution of sensibility on either side. The calf muscles are flabby, but there is not much loss of power. He can stand on tip-toe easily. Measurement in thickest part of calf, 13⅝ in.

Very slight if any diminution of faradic irritability, no galvanic changes.

The symptoms in this case point strongly to some lesion of the nerve trunks, and the heredity would indicate something more than an accidental neuritic origin. It is very probable that this is an early

case of the type under consideration, but at present the atrophy is such a subordinate feature, that the case has not been included among the above statistics.

The last factor in the symptomatology to be noticed is the *electrical condition* of the muscles. As in the myelopathic type, so in this, the wasting of the muscles is accompanied by a corresponding diminution of the irritability to the faradic current. But in the peroneal type there is a comparatively early tendency to the reversal of the polar reactions to the continuous current. This is not the case in the thenar form, in which, reaction of degeneration, if it occur at all, is always a late phenomenon.

The pathogeny of the disease is at present doubtful. Of the cases at present collected, there is recorded a *post-mortem* examination in four. These are so important as to deserve special notice here.

The first is given by Virchow (Table, 2) in 1885. In this no atrophy of the anterior horns of the gray matter was made out, but the posterior columns were gray in colour, the degeneration reaching out each side to the posterior horns. The roots and nerves were not diminished to the naked eye, but in section the fibres were seen to be separated from one another by a growth of connective tissue. The fine nerve branches do not seem to have been examined.

In the second, by Oppenheimer, (Table, 3) the

evidence is principally negative. The existence of fibrillar tremors, and absence of hypertrophy of any muscles, precludes the diagnosis of pseudo-hypertrophy. The spinal cord was quite free from disease, but the state of the nerves was not noticed.

Friedreich supplies the third (Table, 6). In this absolutely no change was found in the central nervous system, but marked lesions were made out in the nerves. In the muscles of the right hand and legs, the nerve branches were found to be full of connective tissue growth, surrounding and pressing on the single nerve fibres. The neurilemma nuclei were greatly proliferated, and the nerve fibres much thinned, their medullary sheaths being atrophied and often interrupted for a considerable extent. This condition was noted in the intra-muscular nerve twigs, and even in the larger mixed trunks, such as the posterior tibial, peroneal, and median, but in a less degree. Even in the largest nerves, the sciatic and the anterior and posterior roots, were found some degenerated nerve fibres. On the other hand the median nerve of the left side, which showed no muscular change, was quite healthy. Friedreich calls this a *chronic interstitial neuritis.*

In the fourth case, also by Friedreich, (Table, 7) there was some degenerative change in the spinal cord, having its seat in the posterior columns, most extensive in the lumbar region, and thinning

off towards the upper part of the cord, till it was a small gray wedge in the cervical region. All the rest of the cord was quite natural. The anterior roots of the lower cord were not diminished in size, but were wanting in lustre and translucency; under the microscope the fibres were found to have a single contour, and a serpentine course. At the same time there was a general infiltration of connective tissue with many nuclei. The same change was found in the lumbo-sacral posterior roots, and could be traced down the large nerve trunks, to the smaller branches in the lower extremities.

This case somewhat agrees with Virchow's. The lesions of the cord in both cases are obviously *secondary*.

It would appear then, that such post-mortem examinations as we can command, point strongly to the conclusion that the disease is a *neuropathy*, using the term in its restricted sense, and that it probably belongs to that class known by the vague generic term, *neuritis*.

Is this conclusion borne out by the clinical aspects of the disease? Of all the diseases of the nervous system, neuritis is the most Protean in its symptomatology, and it would be out of place here, even if space allowed, to enter, ever so cursorily, upon such a subject. But it must be allowed that while there are no serious objections to the neuropathic hypothesis, there are one or two points in its favour.

In the true myelopathic type, the order of the muscles affected, indicates the progress of the lesion in the gray matter, spreading upwards and downwards from a focus somewhere in the region of the first or second dorsal roots, which centre, as Ferrier and Yeo* have shown experimentally, and Beevor† clinically, controls the muscles of the hand. Here is a distinct continuity between a central cause and a peripheral effect. Such a sequence is constantly wanting in the peroneal type, where the legs are affected first, and then, at a comparatively early period, the hand or arm muscles, the intervening trunk muscles, being apparently unaffected. This condition is difficult to account for by a central hypothesis, except on the supposition of two distinct lesions; while, on the other hand, it is very common in so-called *multiple neuritis*, which has received so much attention lately, especially from Leyden,‡ Grainger Stewart,§ Webber,‖ and Buzzard.¶

Pain, especially along the course of nerves, points to the probability of direct nerve affection. This symptom, however, does not so often occur as it does in the ordinary forms of neuritis, in explanation of which it must be remembered that the disease

* Ferrier and Yeo, *Proc. Roy. Soc.*, 1881.

† Beevor, *Med. Chir. Trans.*, 1885.

‡ Leyden, *Zeitschr. für Klin. Med*, I., 1880, p. 387.

§ Grainger Stewart, *Edin. Med. Journ.*, 1881, p. 865.

‖ Webber, *Arch. of Med.*, N.Y., 1884.

¶ Buzzard, "Harveian Lectures," *Lancet*, Nov., 1885.

probably attacks first the small muscular branches, the main trunks, and with them the sensory nerves, being attacked at a later stage.

The importance of an early appearance of reaction of degeneration, without motor-paralysis, has already been insisted upon.

The true diagnostic significance of *fibrillar* or *fascicular tremors* appears to be as follows. These tremors are conspicuous by their absence in true myopathies; they are very often present in the peroneal type, and nearly always in atrophies due to central origin. They were present in two of the cases (Table, 3,7) in which neuritis was demonstrated *post-mortem*. Moreover, distinct fibrillar tremors are recorded in a case of true idiopathic neuritis by Joffroy,* which was verified by *post-mortem* examination. Fibrillar tremors then serve only to distinguish myopathies on the one hand, from atrophies due to *nervous* lesions, whether central or peripheral, on the other.

From the above related facts may be deduced these conclusions.

1. That there is a form of Progressive Muscular Atrophy, which commences in the lower extremities, most often in the peroneal muscles, but sometimes also in the tibialis anticus, extensor longus digitorum, or gastrocnemius.

2. That the hand and forearm muscles are attacked at an early period.

* Joffroy, *Arch. de Physiologie.*, 1879, p. 172.

3. That the disease is one of childhood.

4. That heredity is a marked feature.

5. That the disease shows a slight preference for the male sex.

6. That fibrillar or fascicular tremors are frequently, but not always, present.

7. That degenerative electrical changes are often an early phenomenon.

8. That from the records of autopsies, as well as from the symptomatology, it may be inferred that the disease is one of the *peripheral nerves.*

TABLE OF RECORDED CASES OF THE PERONEAL TYPE OF PROGRESSIVE MUSCULAR ATROPHY.

No.	Reference.	Sex and Age at Onset.	Heredity.	Order of Affection of Muscles.	Musculo-Motor and Sensory Phenomena.	Electrical Reactions.	Remarks.
1.	*Aran.* Gaz. des hôp. 1855, No. 74.	M. 11.	Two aunts died of muscular atrophy.	Began in R. leg then L. 8 years after. Then R. arm and shoulder muscles, but not hand muscles.	No fibrillar tremors.		
2.	*Virchow.* Virch. Archiv. 1855.	M. 21.	Father died of same disease, æt. 40.	Legs first. Upper extremities later	No mention made.		History very scanty. *P.M.* No affection of ant. horns. Some degeneration of post. columns. Interstitial changes of some peripheral nerves.
3.	*Oppenheimer.* Ueber progressive fettige Muskelentartung. Heidelberg 1855 Canstatt's Jahresbericht, 1855.	2 M. 11. 10.	One other brother, two male cousins, two uncles, suffered with same affection.	Legs much wasted first. Flexors of foot and extensors of thighs gone. Then back muscles. Hands very weak.	Marked fibrillar tremors. Occasional cramps in calves.	Loss of farad. irritability in calf muscles.	Some contracture of calf muscles. 1st. case. *P.M.* No disease of cord or roots found, nerves not examined. 2nd. case. Scantily reported but seems to resemble first. No P.M.
4.	*Bamberger.* Oesterr. Ztg. für prakt. Heilk., 1860. Canstatt, p. 88, 1860.	2 M. 7. 11.	Two brothers. Paternal aunt died of wasting of extremities. Maternal aunt and uncle had some affection of legs. Mother, contraction of legs. Sister, wasted forearms.	Extreme wasting of muscles of legs. Also of arms.	No mention made.	Dim of farad. irritability in proportion to wasting.	
5.	*A. Eulenburg.* Virch. Archiv. 1871.	3 F 8 in each case.	Three sisters æt. 16, 12, and 9, when seen, no other heredity.	Legs first, great wasting of thigh muscles. Hand muscles affected early. Also shoulder and upper arm muscles.	No mention made.	Dim. of farad. irritability in all affected muscles with R. D. in [illegible]	Contractures of knee and hip muscles, also talipes equinovarus.

No.	Reference.	Sex and Age at Onset	Heredity.	Order of Affection of Muscles.	Musculo-Motor and Sensory Phenomena.	Electrical Reactions.	Remarks.
6.	*Friedreich.* Ueber progr. Muskelatroph. 1873. (Case I.)	F. 5.		Right leg, then left. Great wasting of right hand muscles.	No mention made.		Extreme pes varus. Contractures of fingers of right hand. *P.M.* Interstitial change in peripheral nerves of right arm and both legs. Spinal cord quite natural.
7.	Do. (Case II.)	F. 10.	One brother affected with same disease (next case).	Legs first, then in arms and hands. Later in shoulder muscles.	Marked fibrillar tremors. Frequent painful muscular contractions.		Talipes (varus?). Contractures of fingers. *P.M.* Interstitial changes of intra-muscular nerves and large nerve-trunks of affected limbs, ant. and post. roots. Secondary degeneration of post. columns of cord, but no other disease of cord.
8.	Do. (Case III.)	M. 12.	Brother of last case.	Legs, especially small foot muscles.	Fibrillar tremors. Shooting pains along limbs.	No reaction to farad. or galv. in affected muscles.	
9.	Do. (Case IX.)	M. 8.		Legs first then gluteal region. Upper extremities affected later.	Fibrillar tremors.	Faradic irrit. dimin. No R. D.	Talipes of left foot, toes clawed. Kyphosis of spinal column. Contracture of hands.
10.	*Eichorst.* Berlin. klin. Wochenschr., No. 42, 1873.	5 M. 5 F. average age, 18.	History of atrophies in six generations. Ten cases under observation extending over three generations.	Lower extremities in all the cases, mostly peronei. Hand muscles attacked later.	No fibrillar tremors, or pains.	Farad. irrit. dimin. in atrophied muscles.	Tendency to talipes varus or equino-varus in most of the cases.

No.	Reference.	Sex and Age at Onset.	Heredity.	Order of Affection of Muscles.	Musculo-Motor and Sensory Phenomena.	Electrical Reactions.	Remarks.
11.	*Osler.* Archives of Med. N. Y., 1880.	M. 46.	Very marked collateral and ascending.	Wasting of whole left leg particularly thigh, buttock, and loins.	Marked twitchings of muscles.		Very interesting genealogical tree extending over 3 generations. No atrophies as yet among the descendants.
12.	*Schultze.* Berlin. klin. Wochenschr. 1884.	1 M. 2 F. 2 in each case.	Two sisters and one brother, æt. 3, 5, 9, when seen; no ascendent heredity.	Peronei muscles, tibial region, extensors, not calf muscles. In the eldest the thigh, thumb and interossei affected later.	No fibrillar tremors. No pains.	Complete R. D. in two cases.	Talipes varus from the beginning. Contracture of hand in eldest; knee-jerk absent in one.
13.	*Ormerod.* Brain, 1884.	F. 6.	Brother and father have the same affection.	Peronei and calf muscles. Five years later, hand and forearm muscles.	No fibrillar tremors.	No reaction to farad. or galv. in affected leg muscles. In left hand ACC = KCC.	In this and the two following cases the atrophy came on after measles. Knee-jerk present on both sides.
14.	Do.	M. 5.	Brother of 13.	Lower extremities, probably peronei first. Hand muscles affected 4 years later.	No fibrillar tremors.	Diminished reaction to farad. Galv. irrit. nil in leg, but fair in thighs.	
15.	Do.	M. 3.	Father of 13 and 14.	R. leg, calf and peronei muscles.	No fibrillar tremors.	Not made out.	The condition has not progressed; the patient is now 56.
16.	*Charcot and Marie,* Rev. de Méd., Feb., 1886.	M. 5.		First noticed pes varus (affection of peronei). Hands attacked 2 years after.	Fibrillar tremors. Subject to cramp in muscles.	R. D. in some of the muscles.	Hands claw-shaped. Knee-jerk feeble.

No.	Reference.	Sex and Age at Onset	Heredity.	Order of Affection of Muscles.	Musculo-Motor and Sensory Phenomena.	Electrical Reactions.	Remarks.
17.	Do.	M. 3.	Brother with same.	Legs first. Talipes valgus. Calf and thigh muscles. Hand muscles later.	Fibrillar tremors.	Not mentioned.	Knee-jerk abolished.
18.	Do.	M. 3.	Brother of 17.	First in peronei muscles Talipes varus. No affection of upper extremities.	Fibrillar tremors.	Not mentioned.	Knee-jerk abolished.
19.	Do.	F. 14.		R. leg first. Calf muscles then L. Five years after hand muscles.	Fibrillar tremors. Cramp in thigh very often.	R. D. in many muscles of the upper extremity. No reaction to galv. in most of leg muscles.	Knee-jerk abolished.
20.	Do.	F. 15.		First in calves and peronei. Four years after, hand muscles began to atrophy.	Fibrillar tremors. Shooting pain in legs.	R. D. in hand muscles. No react. to galv. in legs.	

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